

### REMARKS

1-3. Claims 1-51 are the pending claims in the present application. Applicants hereby cancel, without prejudice, claims 5, 6, 8, 10, 11, 12, 16, and 22. Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

4. Applicants note with appreciation that the rejection under 35 U.S.C. 101 has been withdrawn.

5. Applicants note with appreciation that the rejection under 35 U.S.C. 112, second paragraph, has been withdrawn.

6-8. Claims 1-12, 16, and 22 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, specifically for not being enabling for in vivo methods of promoting the survival of dopaminergic or GABA-nergic cells using small molecules or for treatments of adults with any *patched* therapeutic. Claims 1-12, 16 and 22 are further rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse these rejections to the extent that they are maintained in light of the amended claims.

Applicants maintain the arguments of record regarding the enablement and written description of methods of promoting neuronal survival using small molecule agonists of hedgehog signaling. Nevertheless, to expedite prosecution of claims directed to commercially relevant subject matter, Applicants have amended the claims to more particularly point out other embodiments of the invention which are outlined in detail in the specification. Applicants' amendments are not in acquiescence of the previous grounds of rejection, and Applicants reserve the right to prosecute claims of similar or differing scope. Reconsideration and withdrawal of this rejection are respectfully requested.

9. Claims 1-3 are rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Hynes et al. Applicants traverse this rejection to the extent that it is maintained in light of the amended claims.

Applicants maintain the arguments of record and contend that the experiments performed by Hynes et al. using early neuronal explants fail to anticipate the claimed invention. Hedgehog signaling has important inductive roles in many developmental systems including the central nervous system and the limb. The experiments of Hynes et al. focus on this early, inductive role of hedgehog signaling. Hynes et al. treated explanted E9 midline tissue comprising midbrain floor plate and the underlying mesoderm with Sonic hedgehog or agonists of PKA. Such E9 explants represent early, pre-differentiation tissue prior to the time when markers of differentiation such as TH are expressed. These experiments highlight the important **inductive** role of **Sonic hedgehog** in the central nervous system. However, these experiments do not address the role of hedgehog signaling in promoting cell survival. In fact, the system used by Hynes et al. cannot reasonably address this question.

Nevertheless, to expedite prosecution of claims directed to commercially relevant subject matter, Applicants have amended the claims to more particularly point out other embodiments of Applicants' invention. Such amendments are not in acquiescence of the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope. Reconsideration and withdrawal of this rejection are respectfully requested.

### CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945**.

Date: January 27, 2003

**Customer No: 28120**  
Docketing Specialist  
Ropes & Gray  
One International Place  
Boston, MA 02110

Respectfully Submitted,



---

David P. Halstead, Ph.D.  
Reg. No. 44,735